

FIG. 1

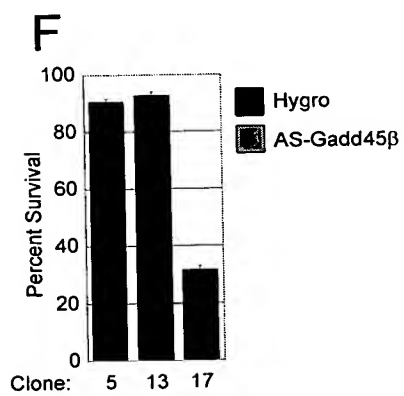
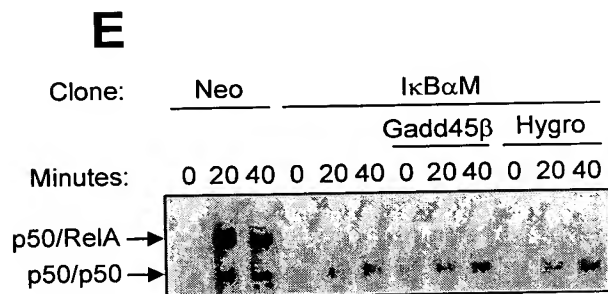
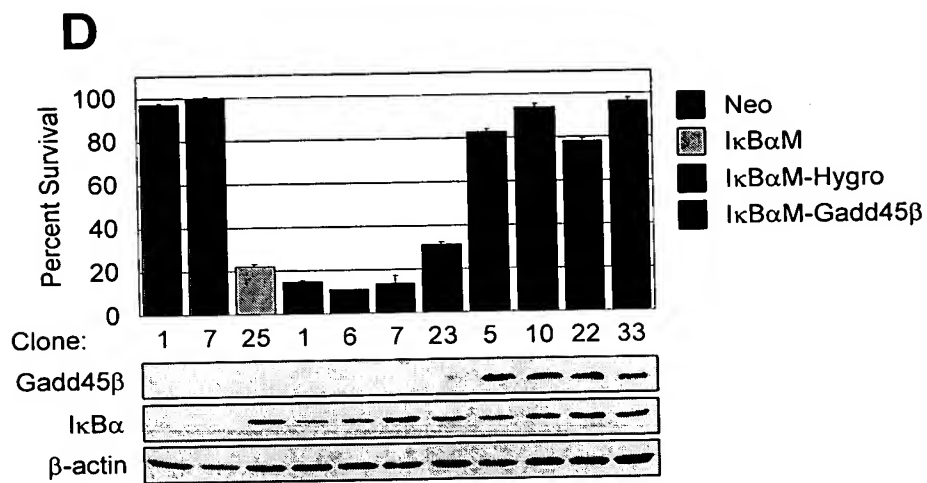


FIG.1 Cont.

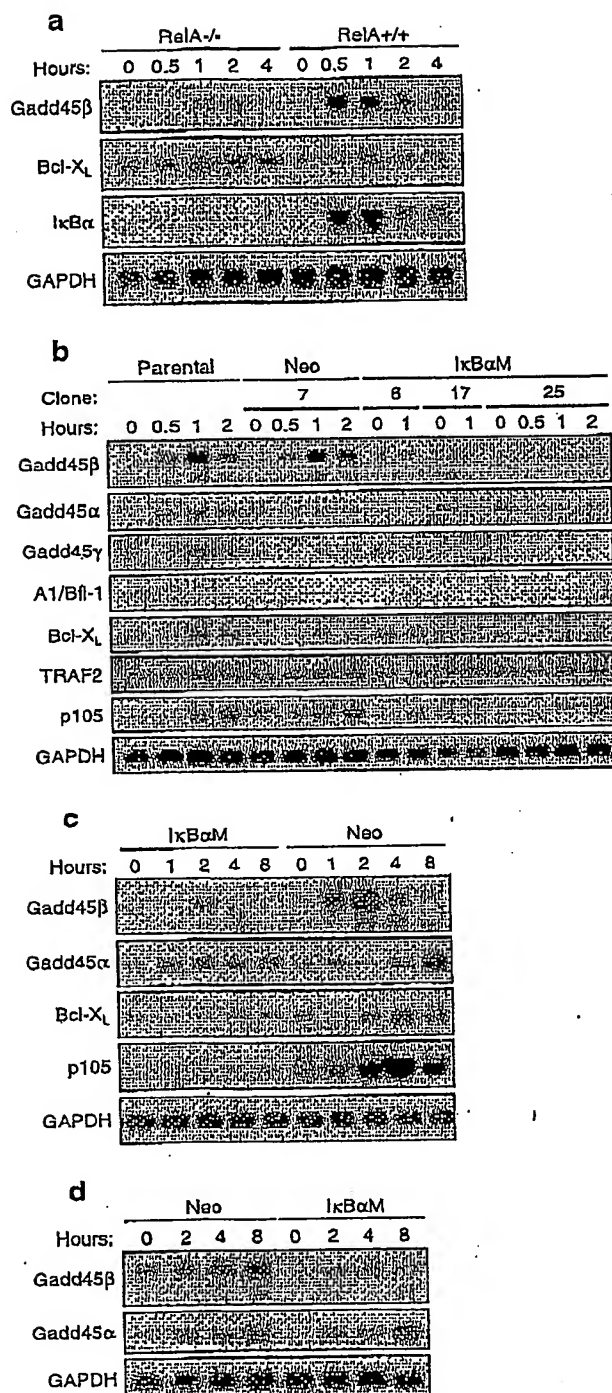


FIG. 2

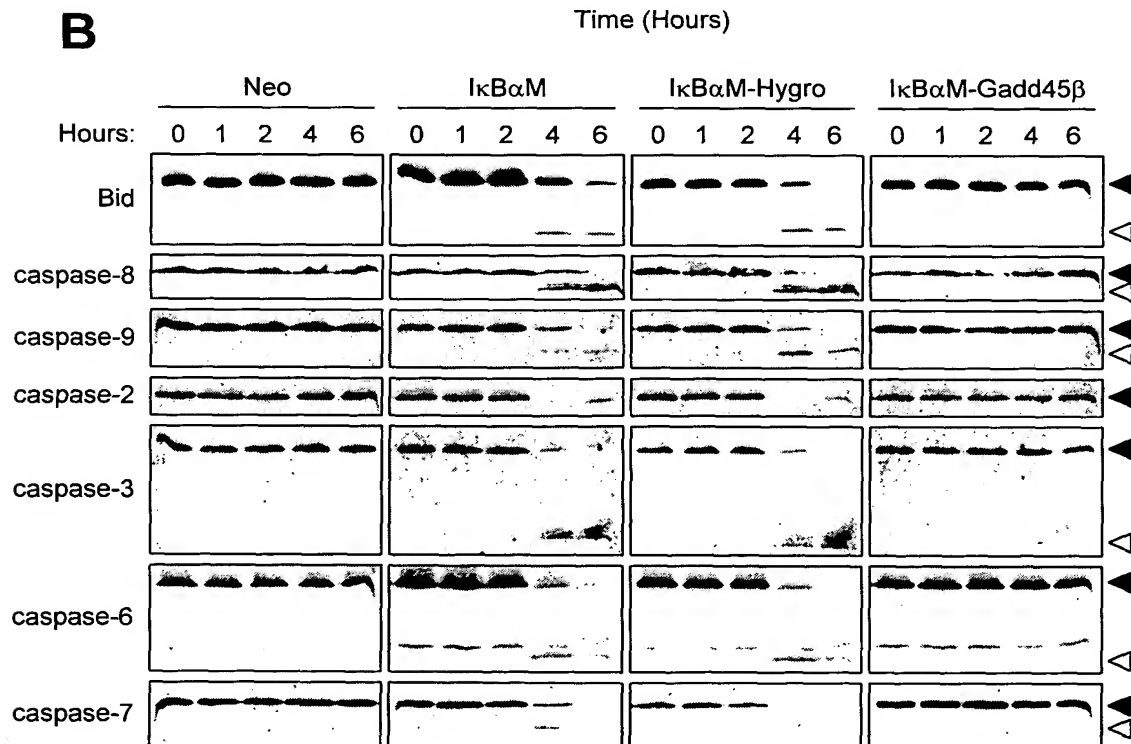
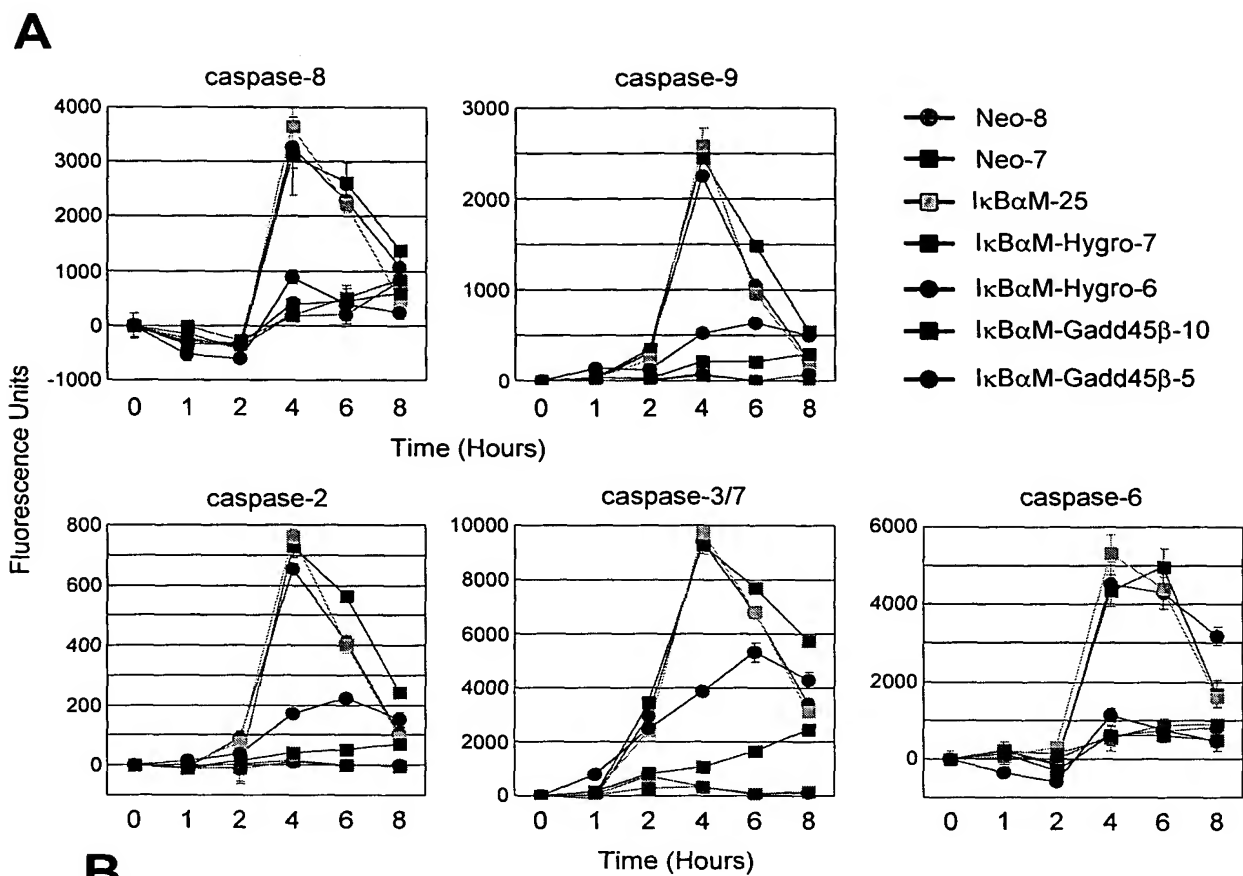


FIG. 3

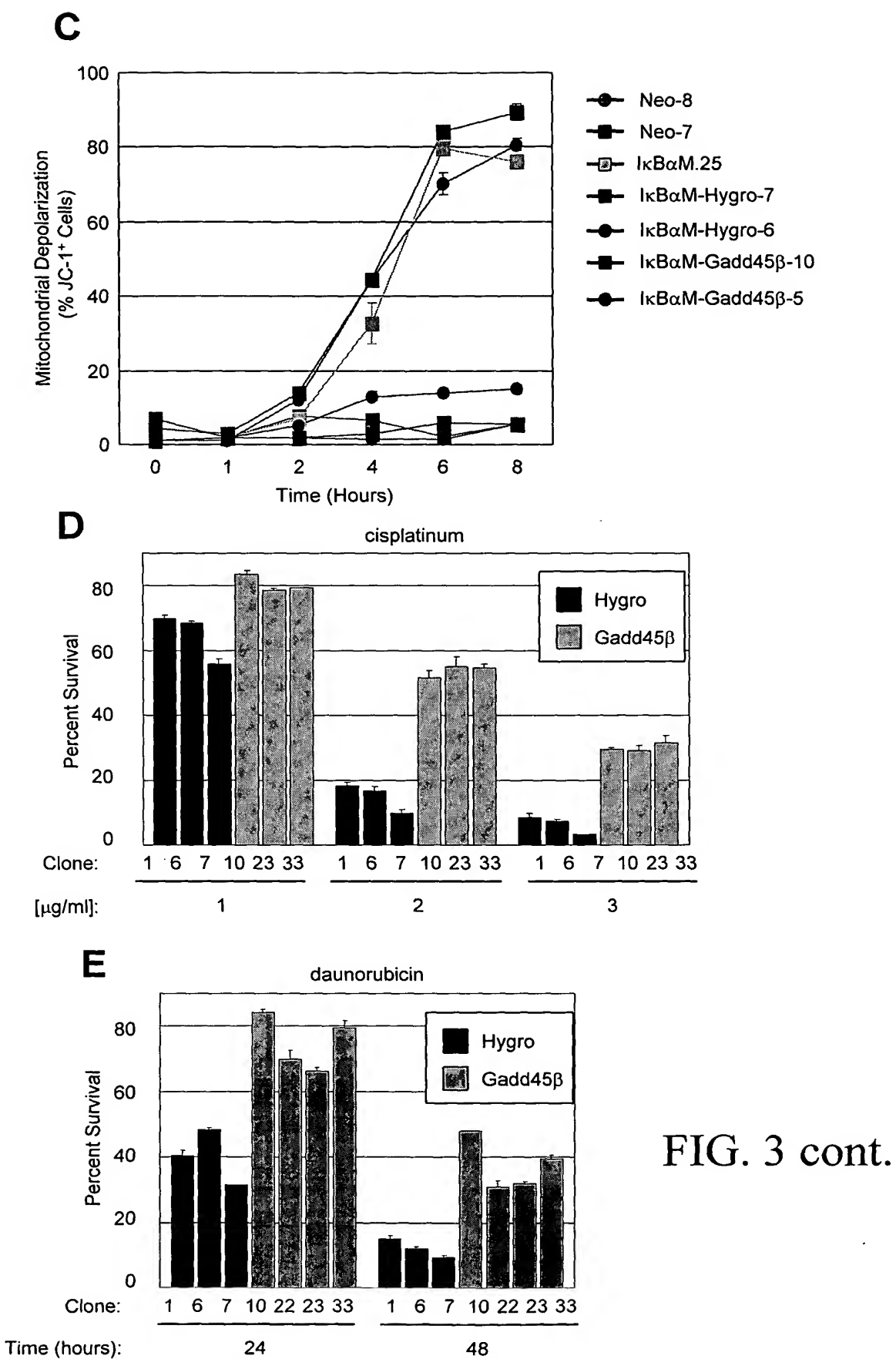


FIG. 3 cont.

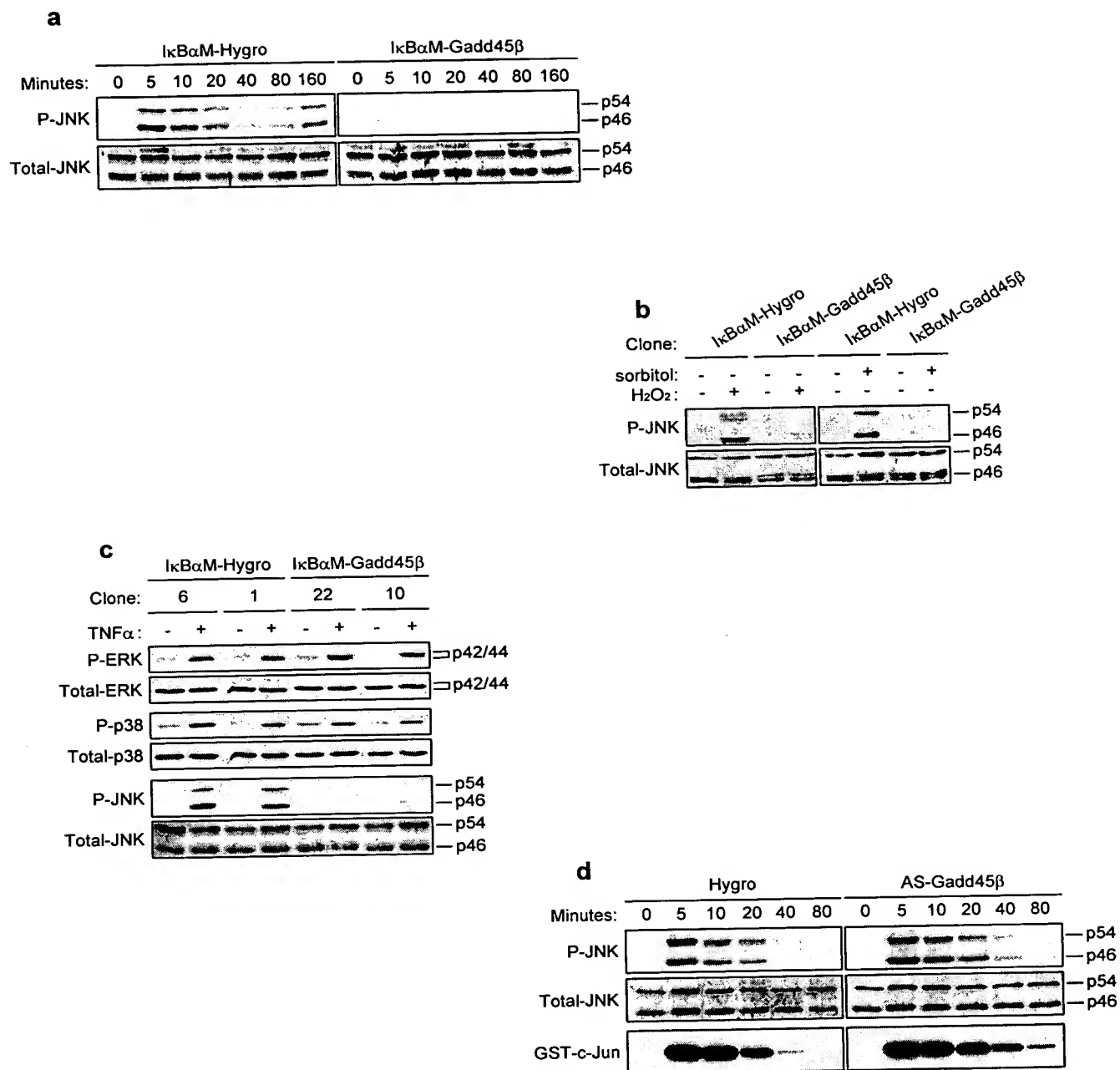


FIG. 4

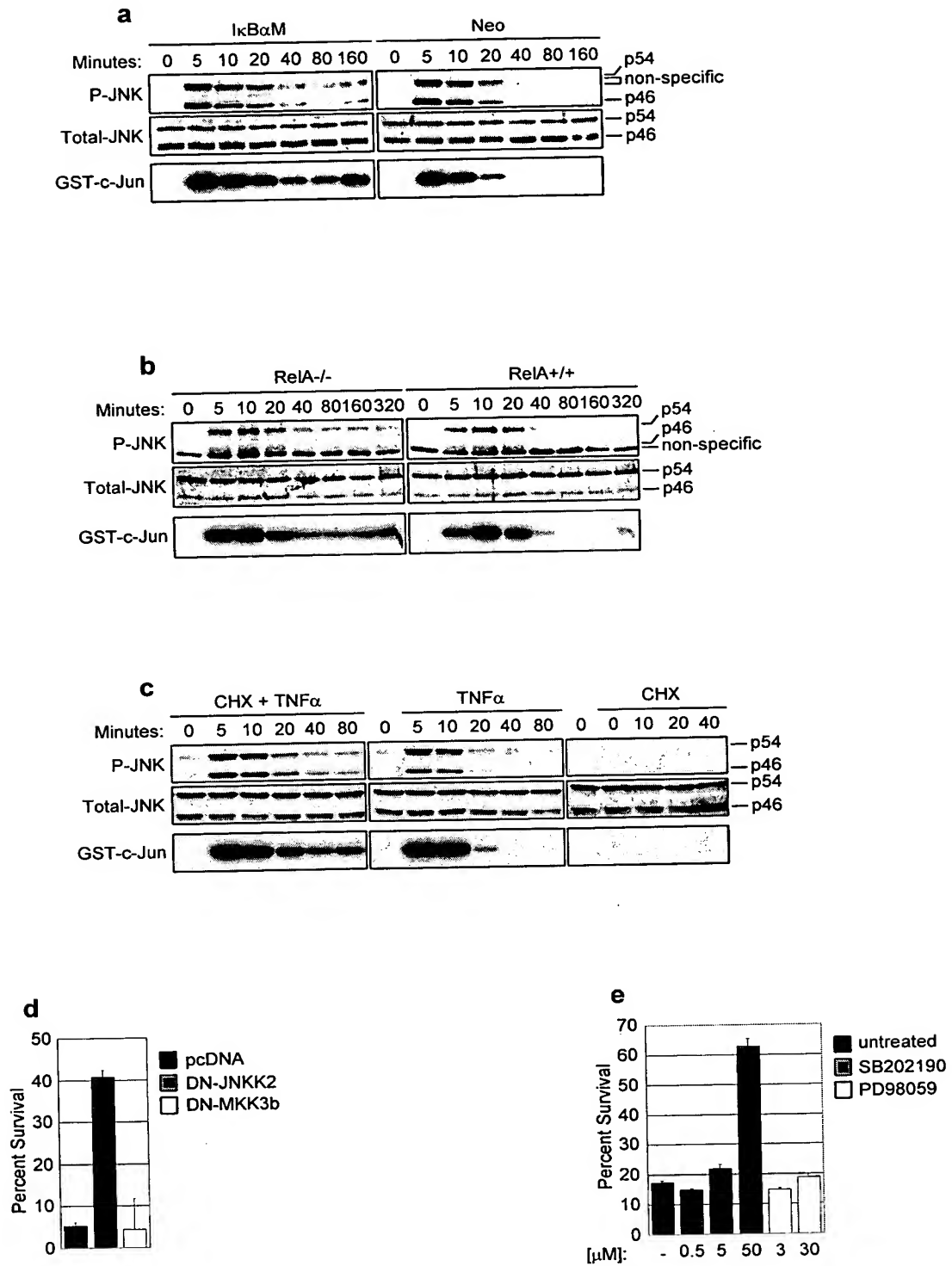


FIG. 5

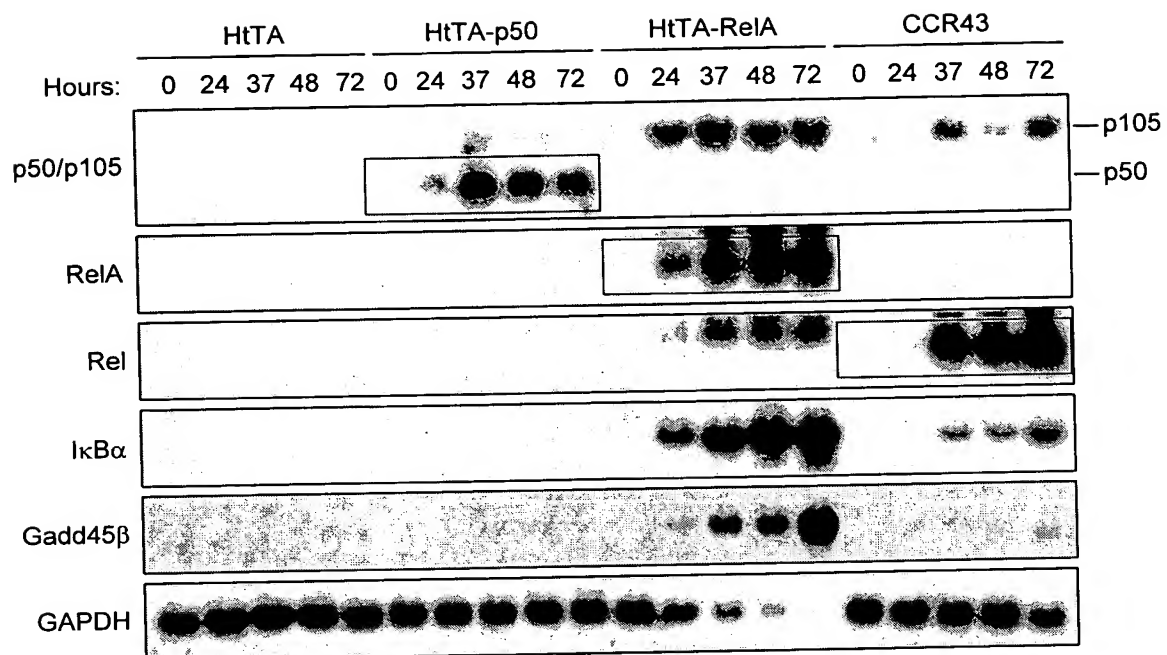


FIG. 6

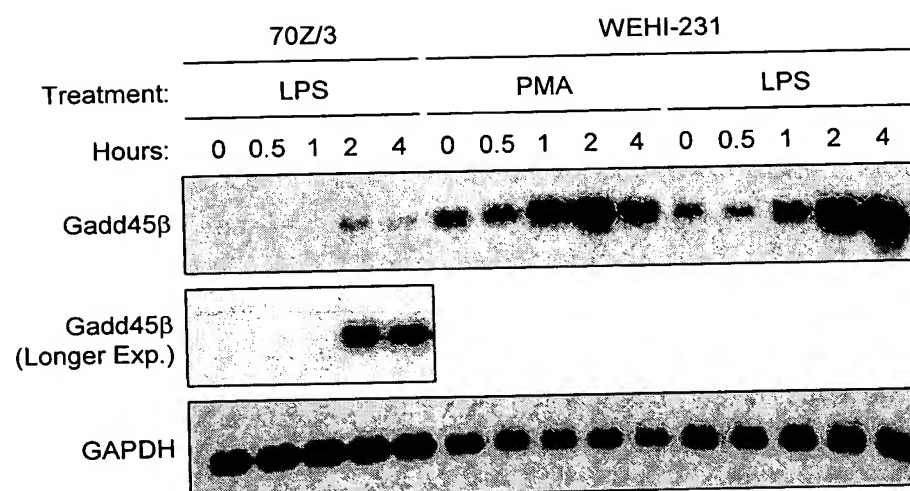
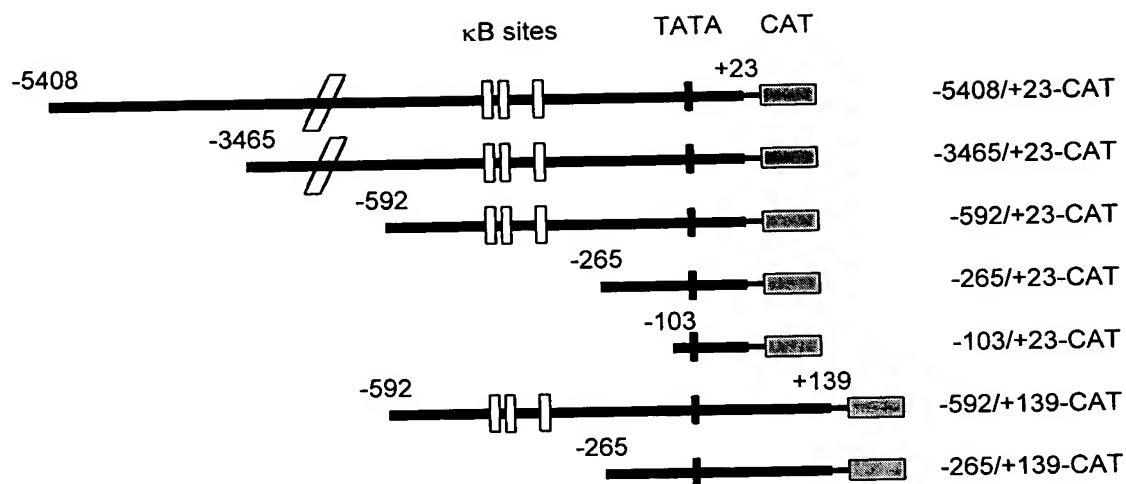


FIG. 7

-2608 GGCCTCTGGG ATTTTGGTTG TGTTTAAATC ATTCCTTTTG ACTTTCTATG TGCATTGGTG TTTTGCCTGT ATGCATGTCT
 -2528 GTGTGAGGGT GTCTGGTCCC CTGAAATTGG AGTTACGGAT GGTGTGAGC TGCCATATTG AACCTGTTC CTCTGGAAGA
 -2448 GCAGCTAGTG CTCTTAATCT CTGAGCCATT TCTCTGCCCC TGCTGTTTGT TTTGCTTTGT CTGTTTTGG TTTCGTTTGG
 -2368 TTTTGGTTTT TCGAGACAGG GTTCTCTGT GTAGCCCTGG CTGTCTCGGA ACTCACTCTG TAGCCCAGGC TGGCCTCGAA
 -2288 CTCAGATATT GCCTGCTCTG TGGTGGCA GT GGTGGG TGAGGGGT GTGCGAC CAC TGCCTGGCAA CAACCAAGTGT
 -2209 TCTTTAAGGC TGAGACATCT CTCTAGCCCC ACCCCAGGT TAAAAACAGG GTCTCATTTA GCCCAGGCTA GTCTCAAAC
 -2129 CACTACATAG CCCTGGATGA TCCTGACCTA CTGACTGATC TTCGGTCTC TTCCTTCTA GGGCTGGGAT GACAAATGTG
 -2049 TACCACCATA GGGTTCGTGT GGTACAGGGG TGGAAAACAG CGCCTCACAC ATGCTCAGTA CGTGCTCTGC CATTGAACCA
 -1969 TTGCTACAGT CCAGCAGCCA ATTAGACTA TTTAAATACA CATCTAGTAA AGTTACTTA TTTGTGTGTG AGGACACAGT
 -1889 ACACTTTGGA GTAGGTACGG AGATCAGAAG ACAATTGCGA GGAGTCAGCT CGAACCTCC ATCCTGTGGA GGATGTCTTG
 -1809 CCCTTCATGT TTGATATTTA AAATACTGTA TGTATAGATT ATTCCAGTT GGGCTATAGC GGTATGTAGA TATTGGTGAT
 -1729 GAGCTTGCTA GGCATCACGA AGTCTGGAT TCATCACCAG CATCGAAAAA AAAATTAATA AAAAAAAAT CGCTGGGCAG
 -1649 TGGTGGCCCA CGCCTTTAAT CCCAGCAAGC ACTAGGGAGG CAGAGGCAGG CGGATCTCTT GAGTTCGAGG CCAGCCTGGT
 -1569 CTACAGAGTG AGTTCAGGA CAGTCAGGC TATACAGAGA AATCTGTCTC AAAAAAAAAA AAAAAAAAAA AATCATTCCA
 -1489 AGTGTCTCTT CCCGCTGCTT TTCCGGAAGC TGCTGAGCA GAGAGCTGAT GAGGGCAGC AGGTGTCGGC GCGCGGCTG
 -1410 TCACGCGAGG GACATTTCGC ATGCT--- G GGTGGGTGGC GCGGAGGAAG CAGGATGGGT CA CCAGACC CGGATCGGG
 -1335 CGATCGGGG ATCGGGGA CC GAGCCGC GC GGC GAGG CCAGGACCA GGCTGGCGGA GGAGC CACT CAG GCTGAT
 -1257 TCAC CCCGGA GCCCCG GTG CACCGTGGGA GA ATCCCA CGC GGGTCT ATG CCCTCG CTCGTCTCT TGCTGTCGAC
 -1182 TACCAGCCCT CAAGCTGTGG CTTGGAACGC CTTGGAGGC CTCAGTTT C GATTTTGCAT AATGCAGATA TCAATTCCTT
 -1103 TGCTGACAA ATCTTGGAAG GATAAATGAC ACGCGTGGAA GAAGGGGCTT GTGCTTCATG CTACGCACTA CAAAATGCC
 -1023 AGGGACATAA GAGCGGCTGC CTTTCAGTCA CCTCTCCCCG GGTCACTACC CTTGGGGTTT TGCCACTTGG CTTCCCCCTC
 -943 AGGGGTTAAG TGTGGCGAAT CGATCTGAGG ATAGACGGTG AGGCAGCCCG CAGGGGGCAG GGTCACTCCG CAGAGCGTCT
 -863 GGAGGGCTCT TCACCTGCGC CTCCCGTGCA CACGTGAAT TCTCGGGGTG CCG GGAGGAG GGAG AAAGGG TTCCGGATCT
 -783 CTCCCCCTGC GATCCCTTAG TGCTCTGCAG CCAGGACCCC TGGGGCACCG CCAAGCCACC TACCAGGACC ACTAGGAAGC
 -703 TTCTGTGTG CCTCTCCTCC CGCGACCCCTG GCCTTAGAGG GCTGAGCGTT CTCAAAGCAC CTTCTGTCTG GCGATGCTAG
 -623 GGTGCCTTGG TAGTTCTCAC TTTGGGGAGA GGATCCACC GTCCCTCAAAC TTACCAAACG TTTACTGTAT ACCCTAGACG
 -543 TTATTTAAAC ACTCTCCAAC TCTACAAGGC CGGCAGAACA CTTAGTAAGC CTCTGGCGC ATGCACATCC CTTCTTTAG
 -463 AGCTTGGGAA AGGC --- T AGGACTCTC CGGGGACAC C GAGGGGATTC CAGACAGCCG TCCCGGAAG TTGAGGCCAG
 -388 CGTCTCGCGC TGGAACCCG GCGCGCGCGC TG --- GTAG CGCGGCTGCC GGGAAATCAG GAG --- AGAAA CTTCTGTGG
 -313 TTTTTTT TT TTTTTTTT TTTTTTTTCT TCTCTAGAGC TCTCTCTTA GAGCTCTCTG GCTTTTCTAG CTGTGCGCGC
 -233 TGCTGGCGTT CACGCTCTC CCAGCCCTGA CGCCACGTG GGG CGCGCG AGCTCCGAGC TCCGCCCTTT CCATCTCCAG
 -153 CCAATCTCAG CGCGGGATAC TCGGCCCTTT GTGCATCTAC CAATGGGTGG AAAGCGCATG CCTCCAGTGG CCACGCCCTCC
 -73 ACCCGGGAAG TCATATAAAC CGTCTGCAGC GCCCGCGCGC TCACTCCGCA GCAACCCTGG GTCTGCGTTC ATCTCTGTCT
 +8 TCTTGATTA ATTTGAGGG GGATTTTGCA ATCTTCTTTT TACCCCTACT TTTTCTTGG GAAGGGAAGT CCCACCGCCT

FIG. 8

A



B

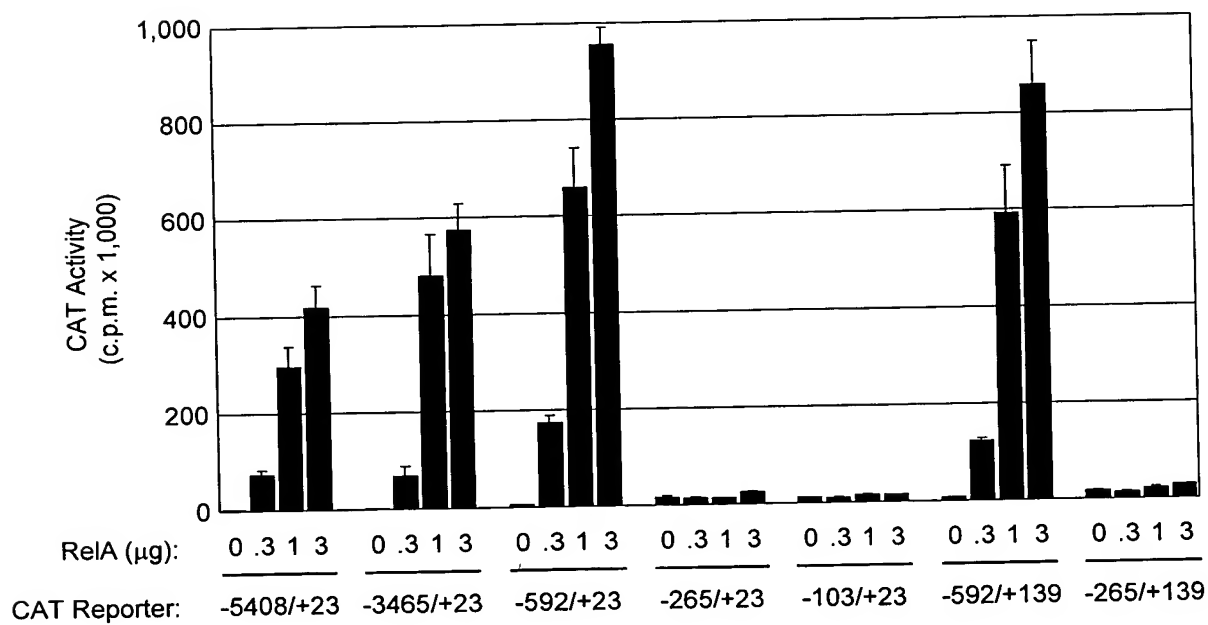
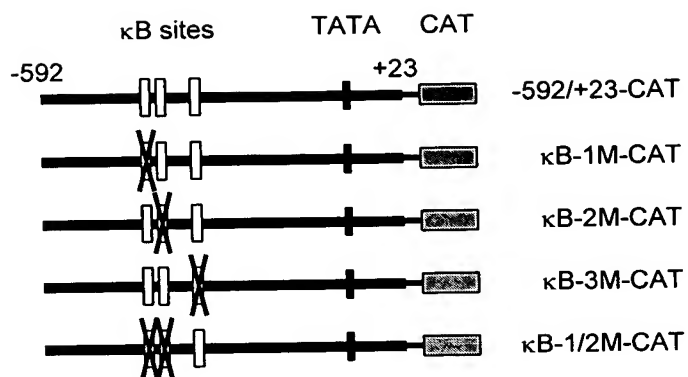


FIG. 9

A



B

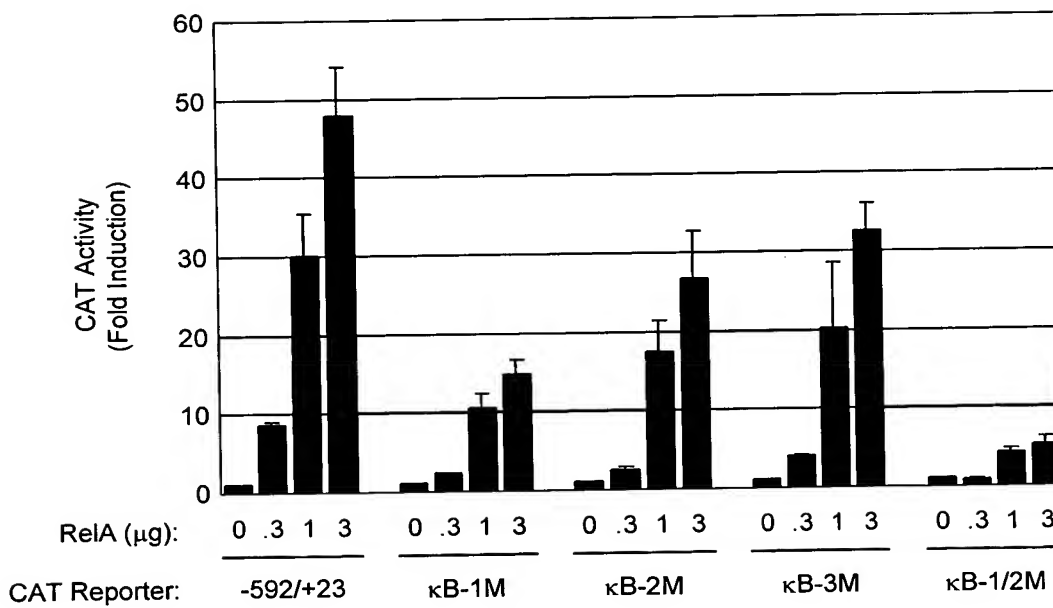


FIG. 10

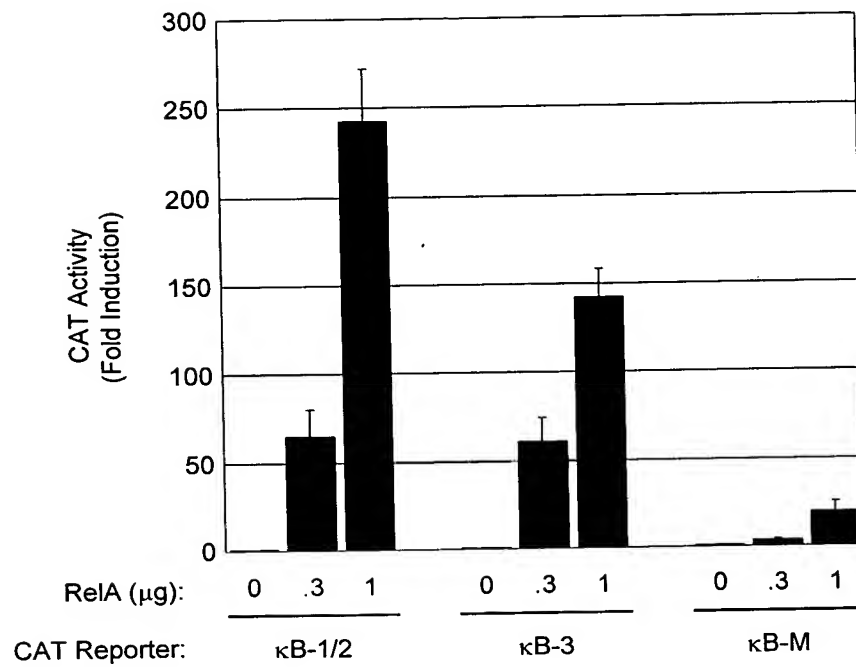


FIG. 11

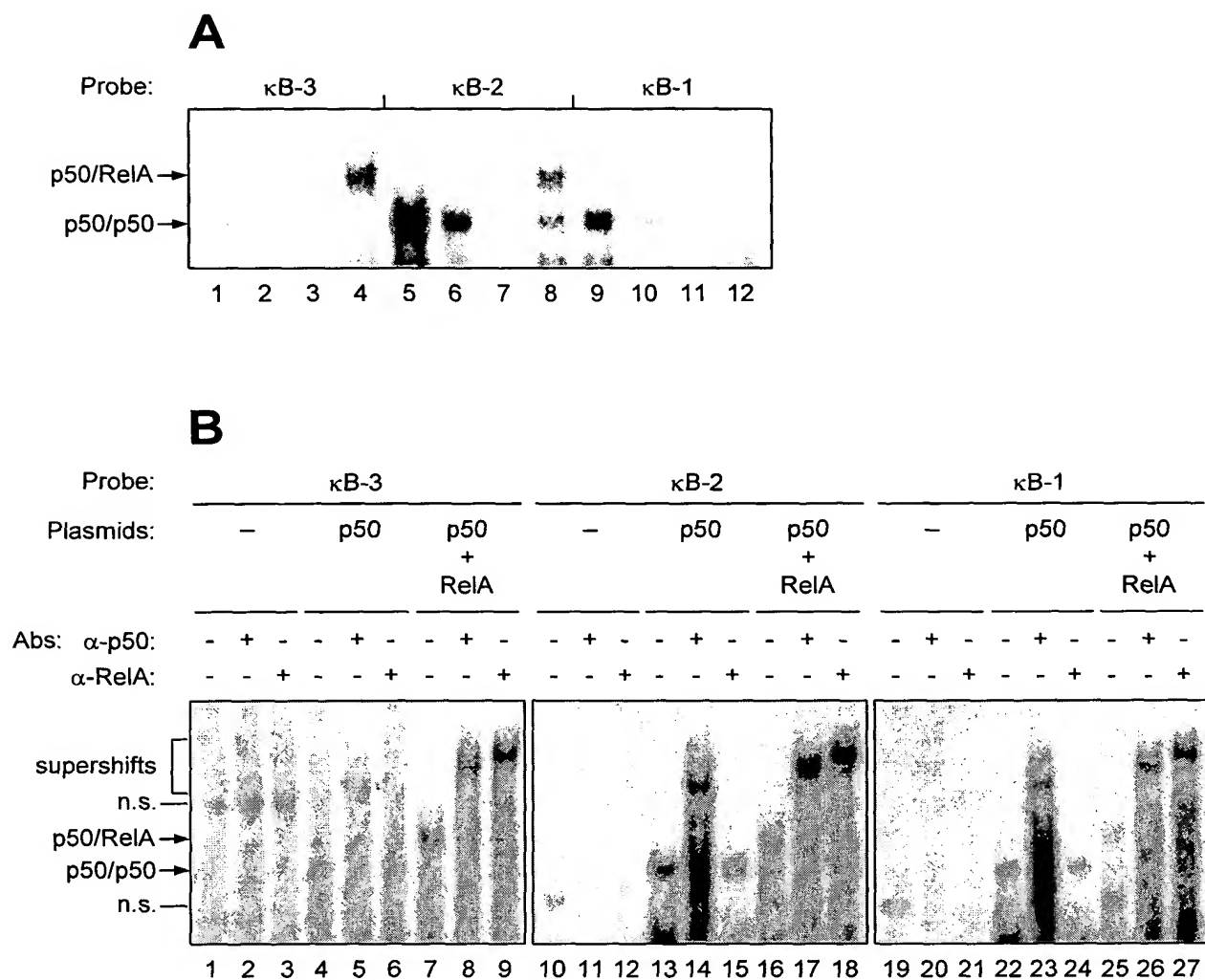


FIG. 12

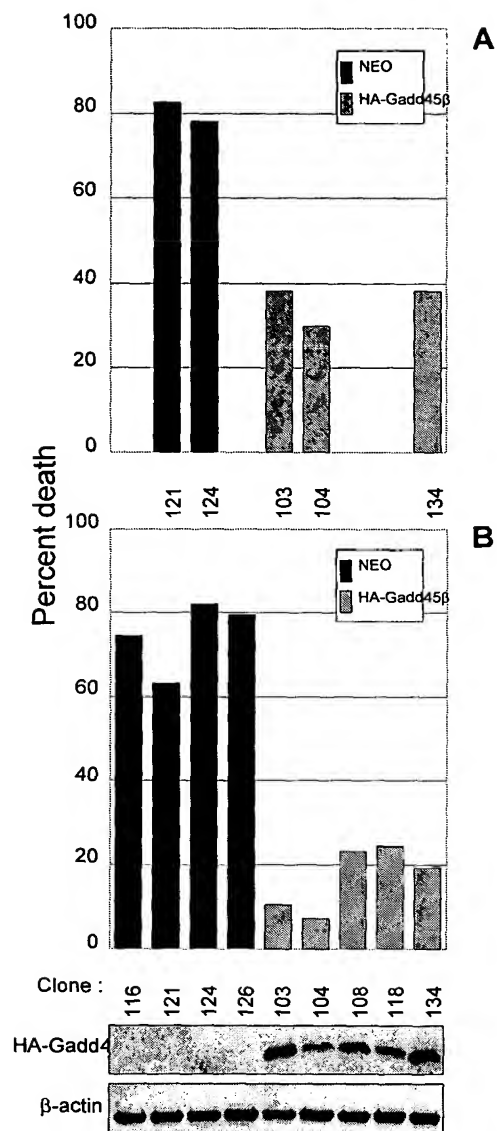


FIG. 13

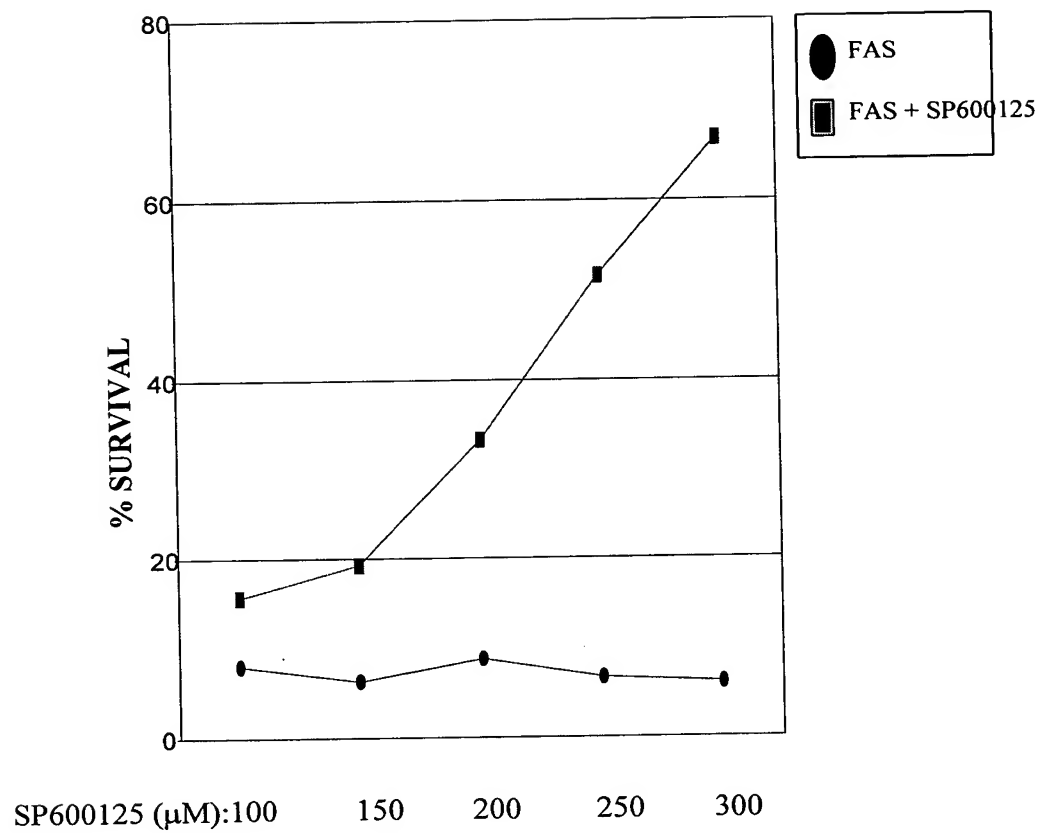
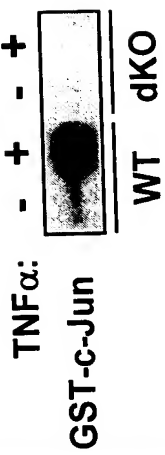
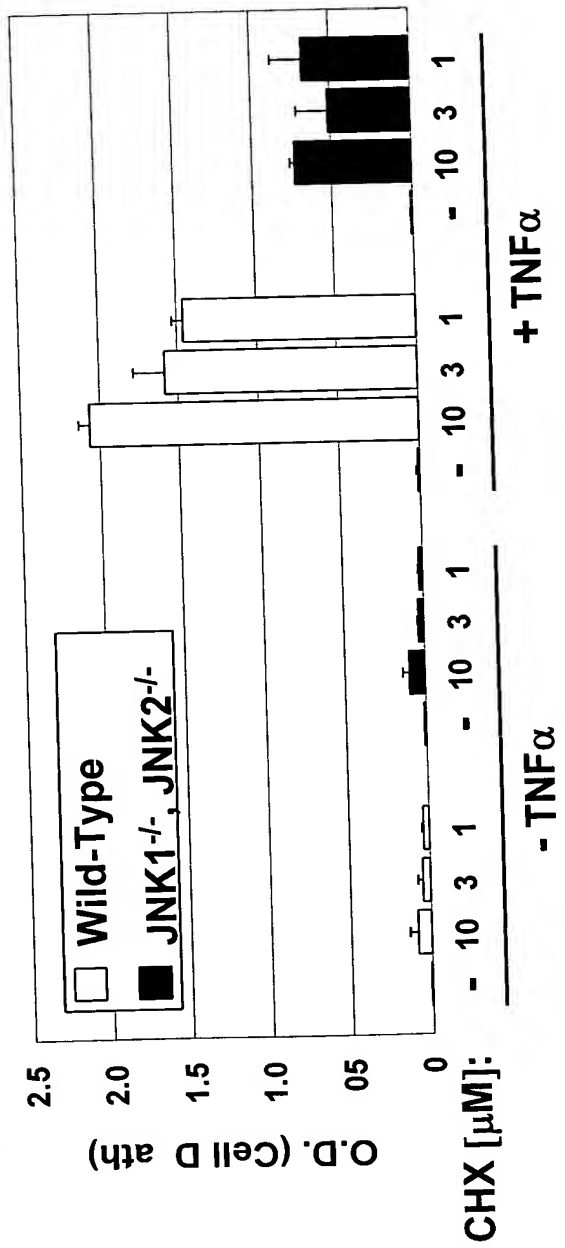


FIG. 14

A



B

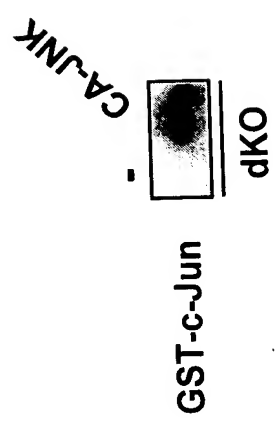
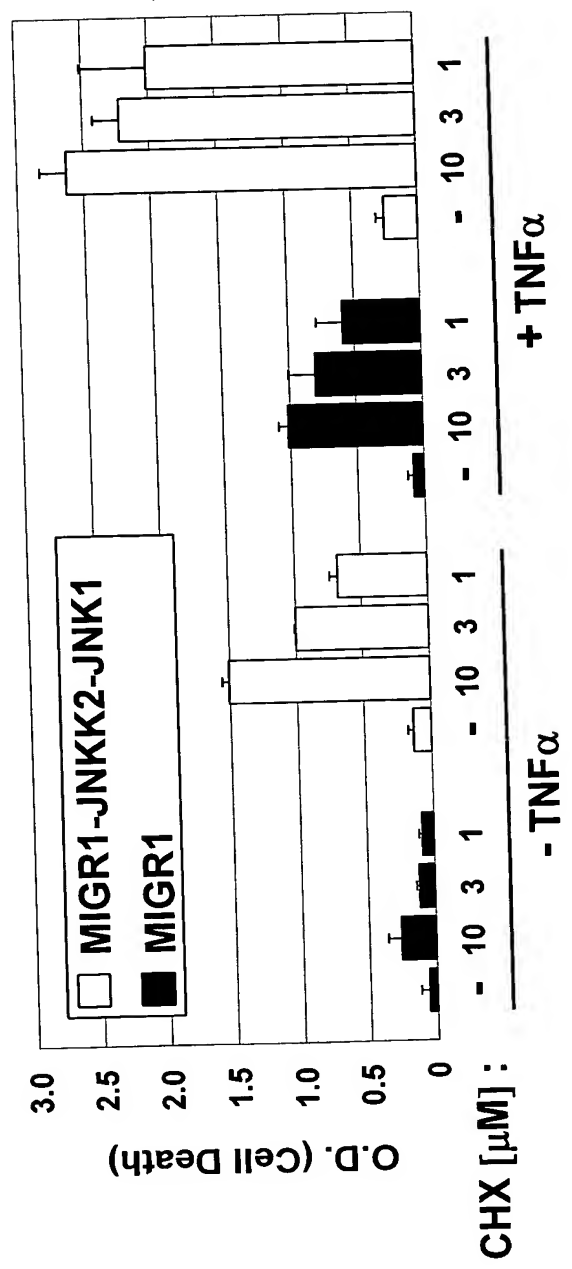


FIG. 15

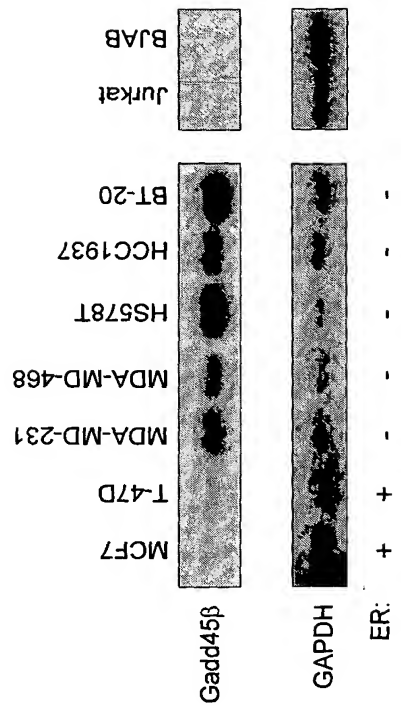


FIG. 16

MDA-MD 231

	SP600125		
	0	100µM	50µM
CAPE (50 µg/ml)	-	+++	+++
Parthenolide (2.5 µg/ml)	-	+++	++++
Prostaglandin A ₁ (100µM)	+	++++	++++

BT-20

	SP600125		
	0	100µM	50µM
CAPE (50 µg/ml)	+	N.D.	+++
Parthenolide (10 µg/ml)	-	+++	++++
Prostaglandin A ₁ (100µM)	+	+++	+++

FIG. 17

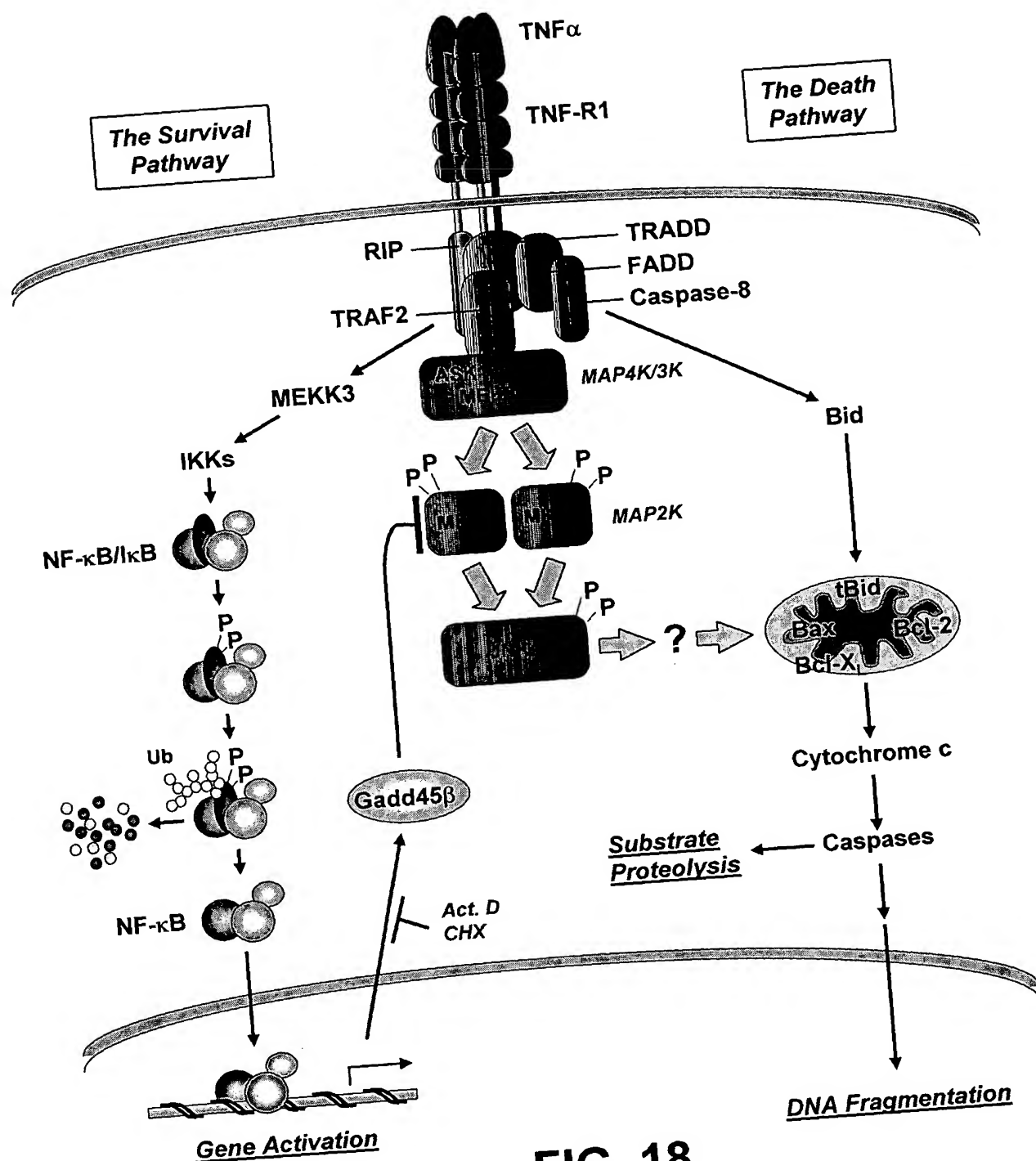


FIG. 18

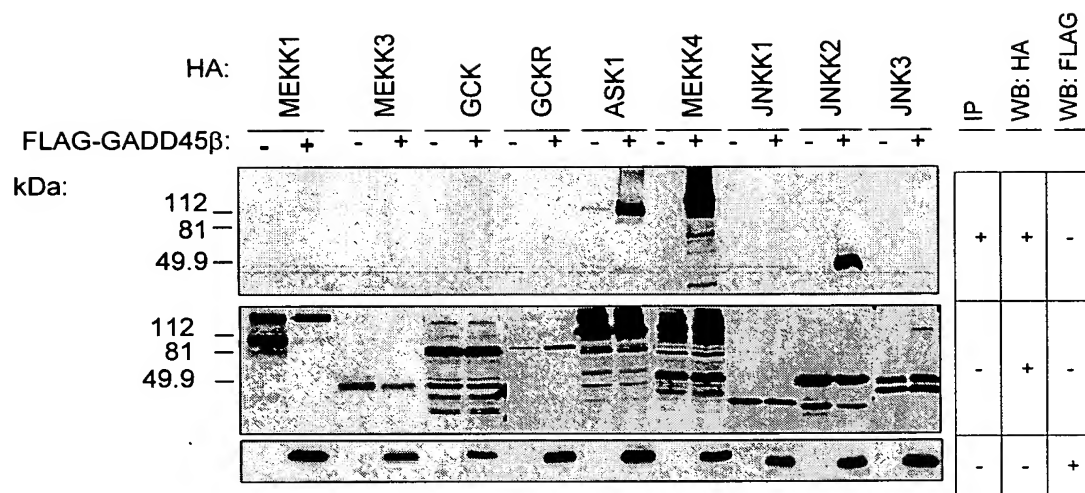


FIG. 19

	MEKK4			JNKK2			JNKK1			C-ASK1			ASK1			N-ASK1		
Input	+	-	-	+	-	-	+	-	-	+	-	-	+	-	-	+	-	-
GST	-	+	-	-	+	-	-	+	-	-	+	-	-	+	-	-	+	-
GST-GADD45 β	-	-	+	-	-	+	-	-	+	-	-	+	-	-	+	-	-	+



FIG. 20

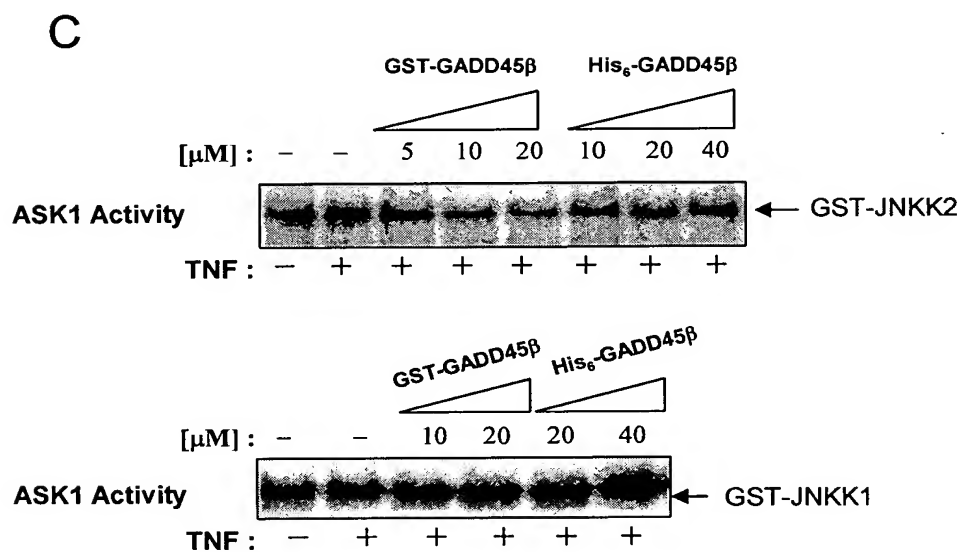
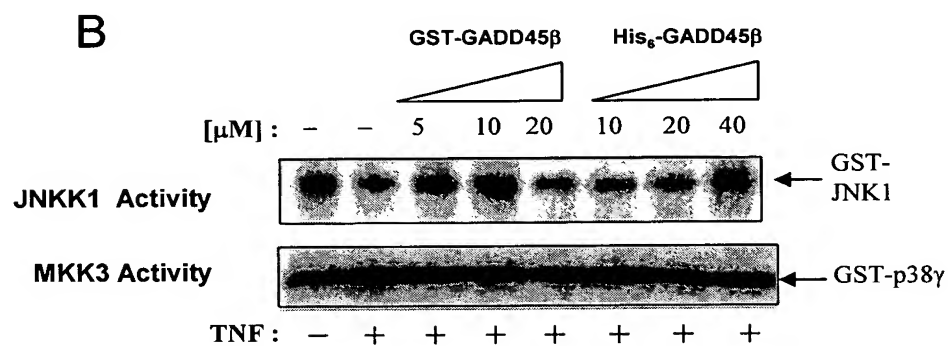
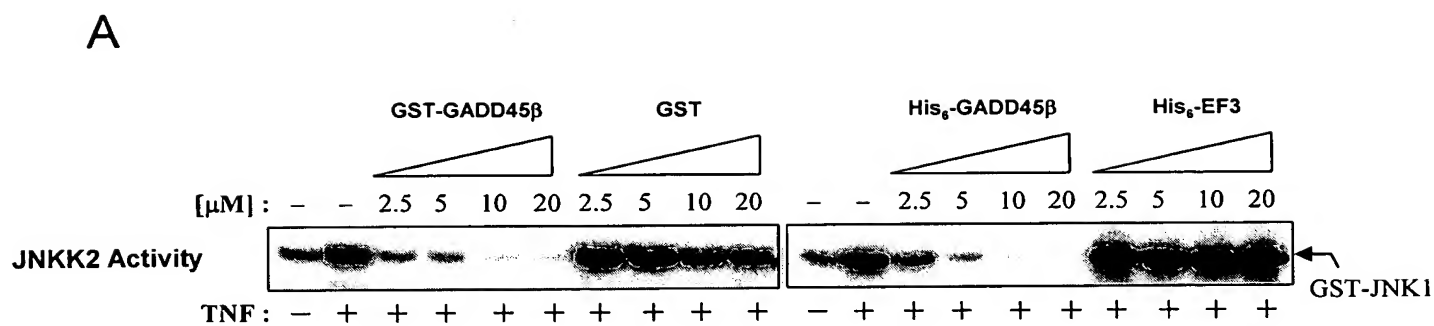


FIG. 21

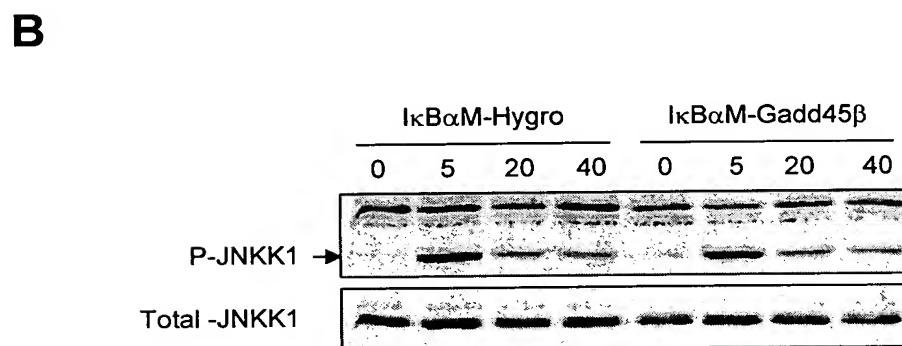
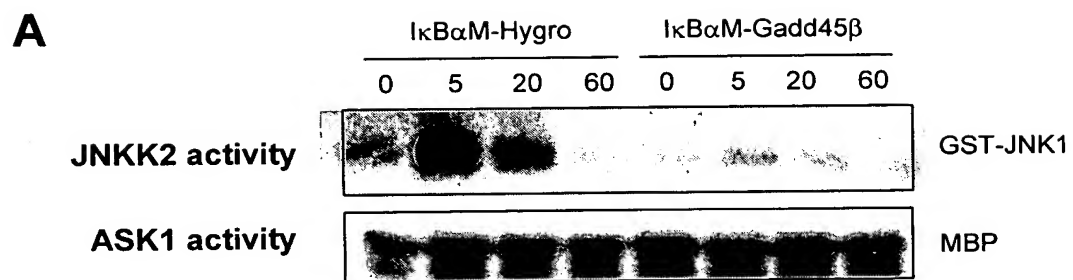
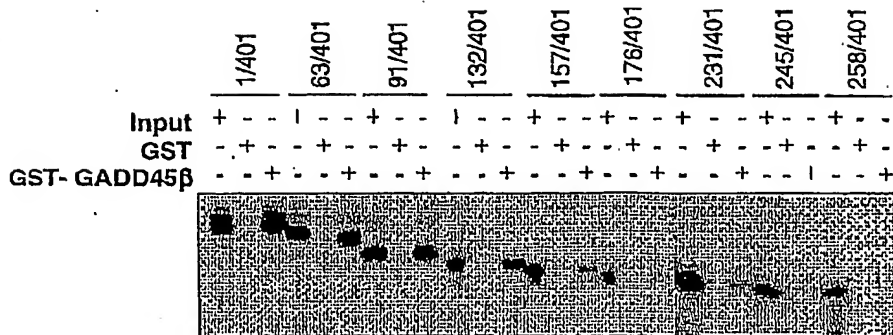


FIG. 22

A



B

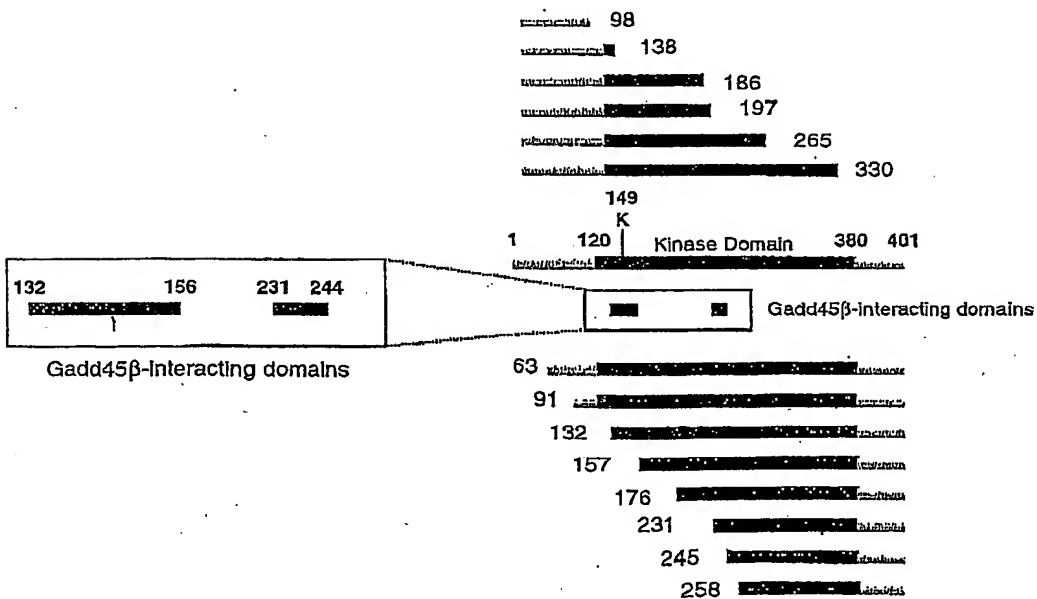
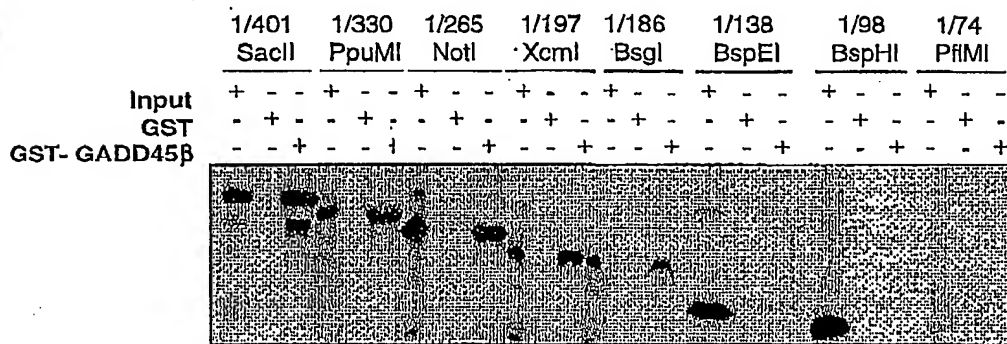
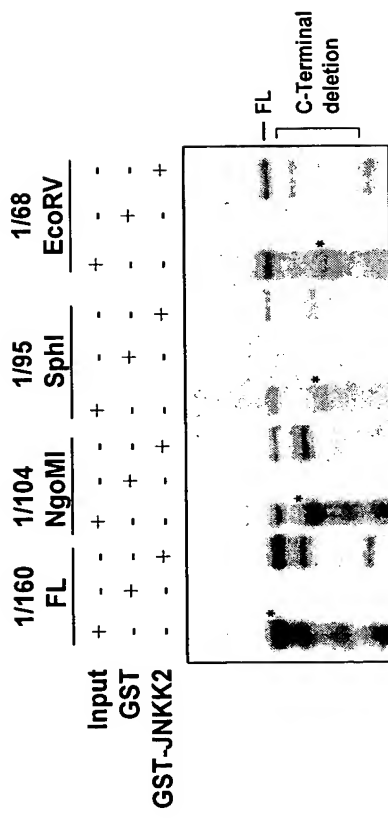


FIG. 23

A



B

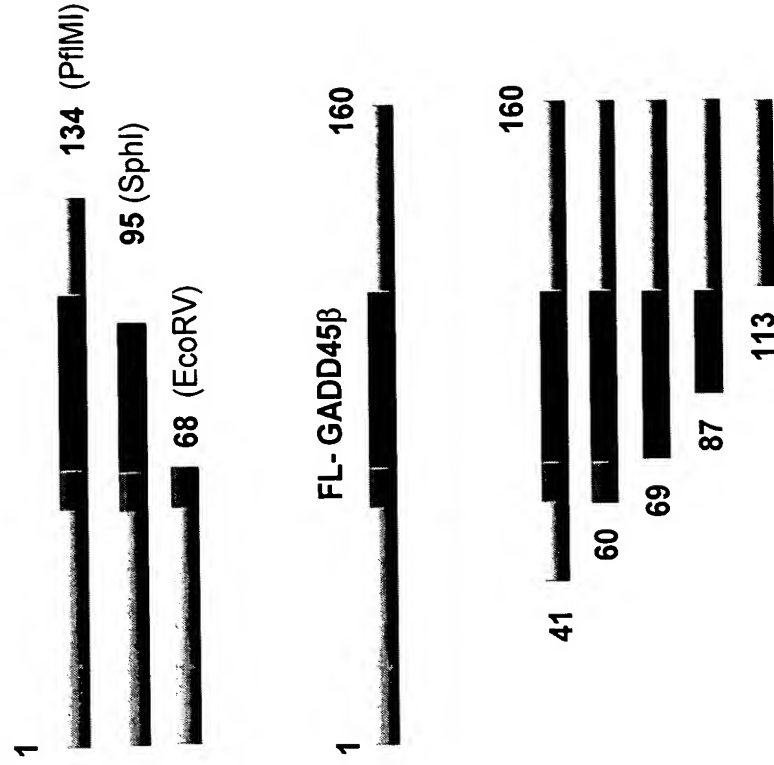
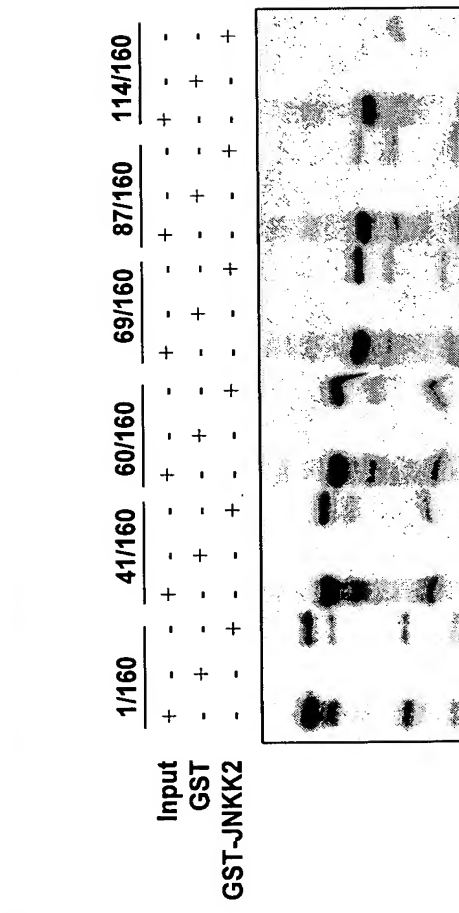


FIG. 24

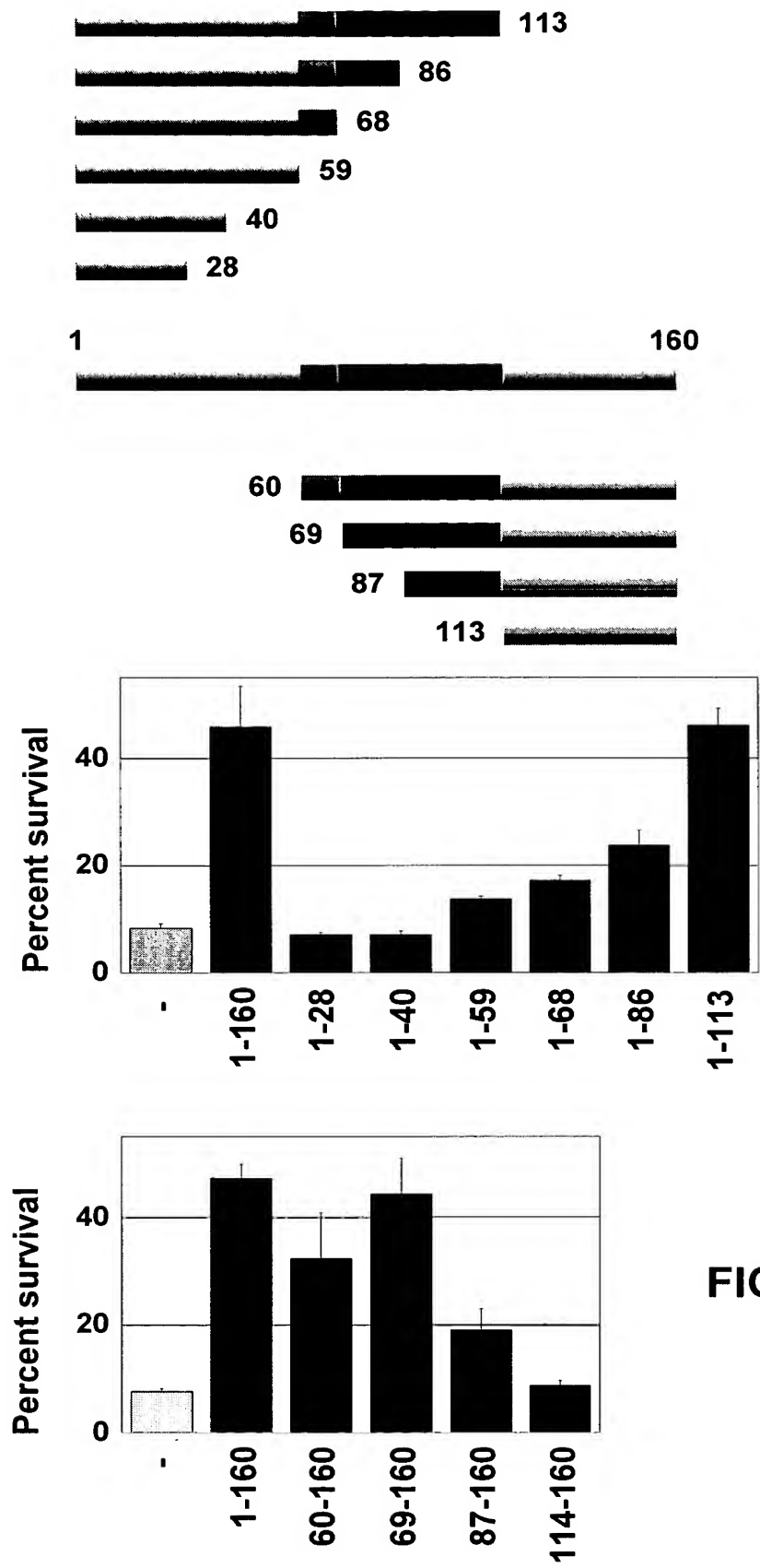


FIG. 25

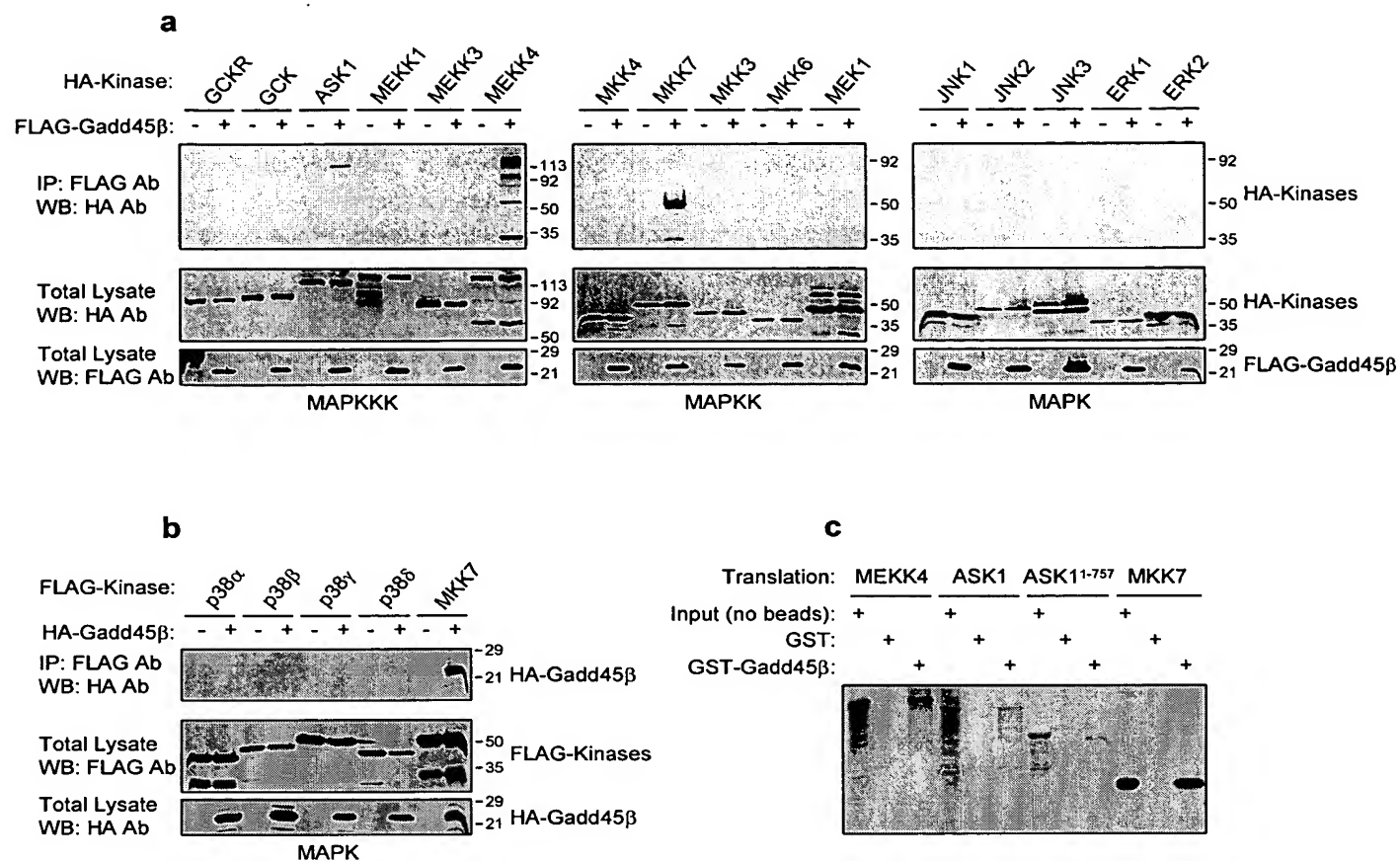


FIG. 26

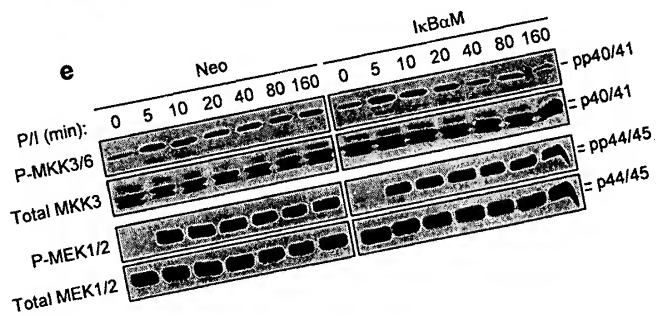
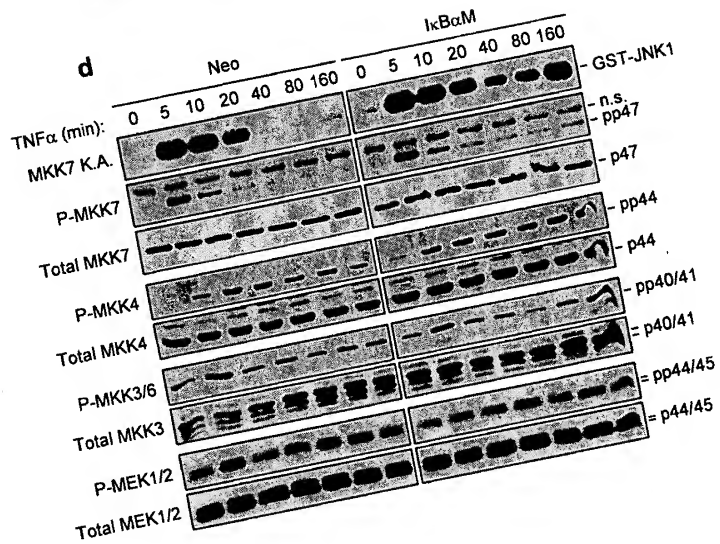
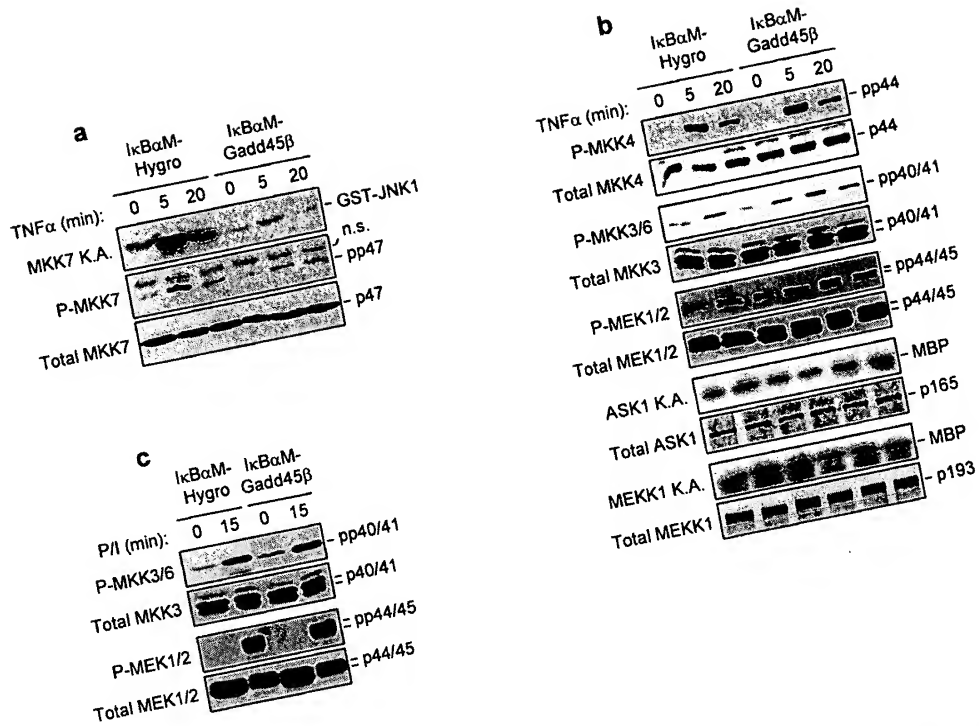
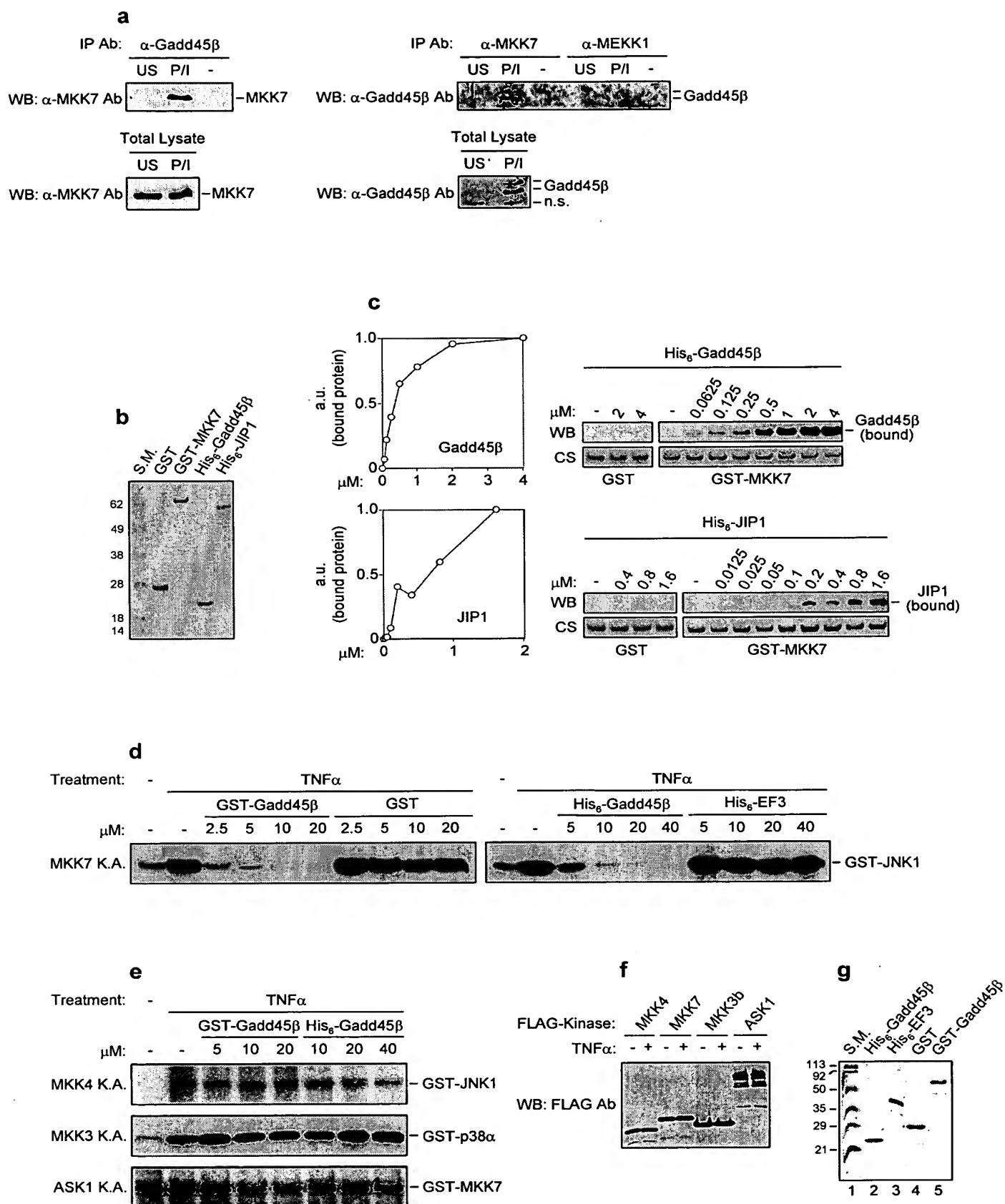


FIG. 27



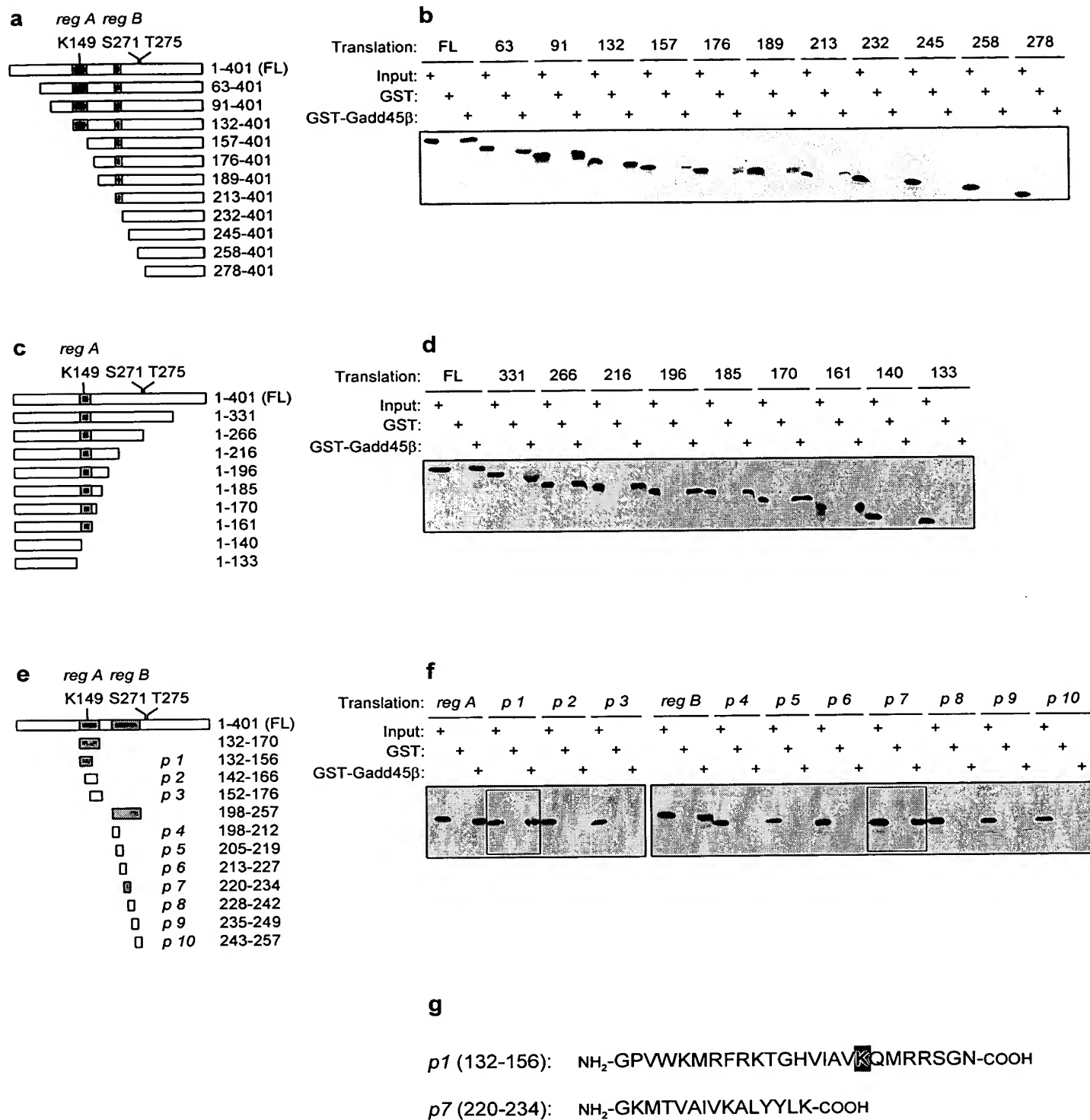


FIG. 29

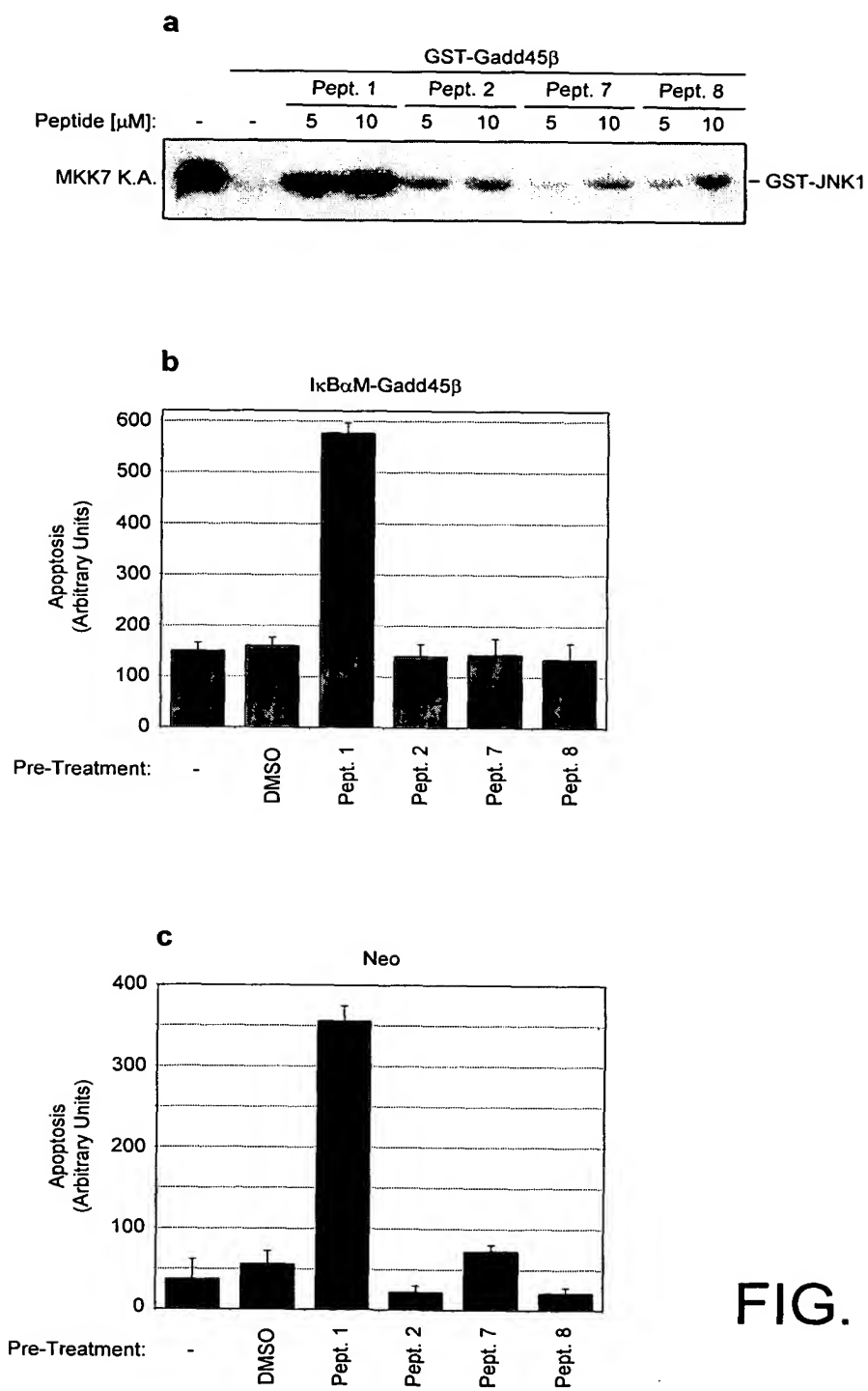


FIG. 30

(A) Homo Sapiens - JNKK2 cDNA
Accession AF006689

```

1 aattcggcac gagtggtttg tctgccggac tgacggggcg cggggcggtg cgcggcggcg
61 gtggcggcgg ggaagatggc ggcgtcctcc ctggaacaga agctgtcccc cctggaagca
121 aagctgaagc aggagaaccg ggaggccccg cggaggatcg acctcaacct ggatatcagc
181 cccagcgggc ccaggcccac cctgcagctc ccgctggcca acgatggggg cagccgctcg
241 ccatcctcag agagctcccc gcagcacccc acgccccccg cccggccccg ccacatgctg
301 gggctcccgt caaccctggt cacaccccgc agcatggaga gcattgagat tgaccacaag
361 ctgcaggaga tcatgaagca gacgggctac ctgaccatcg ggggccagcg ctaccaggca
421 gaaatcaacg acctggagaa cttgggcgag atgggcagcg gcacctgcgg accggtgtgg
481 aagatgcgct tccggaagac cggccacgtc attgccgtta agcaaatgcg gcgctccggg
541 aacaaggagg agaacaagcg catcctcatg gacctggatg tgggtgctgaa gagccacgac
601 tgcccctaca tctgacagtg ctttgggaag ttcatcacca acacggacgt cttcatcgcc
661 atggagctca tgggcacctg cgctgagaag ctcaagaagc ggatgcaggg ccccatcccc
721 gagcgcattc tgggcaagat gacagtggcg attgtgaagg cgctgtacta cctgaaggag
781 aagcacggtg tcatccaccg cgacgtcaag ccctccaaca tcctgctgga cgagcggggc
841 cagatcaagc tctgcgactt cggcatcagc ggccgcctgg tggactccaa agccaagacg
901 cggagcgccg gctgtgccgc ctacatggca cccgagcgca ttgaccccc agacccccacc
961 aagccggact atgacatccg ggccgacgta tggagcctgg gcattctcgtt ggtggagctg
1021 gcaacaggac agtttcccta caagaactgc aagacggact ttgaggtcct caccaaagtc
1081 ctacaggaag agcccccgct tctgcccgga cacatgggct tctcggggga cttccagtcc
1141 ttcgtcaaag actgccttac taaagatcac aggaagagac caaagtataa taagctactt
1201 gaacacagct tcatcaagcg ctacgagacg ctggaggtgg acgtggcgct ctggttcaag
1261 gatgtcatgg cgaagacctg agtcaccgcg gactaacggc gttccttgag ccagccccac
1321 cttggcccc tcttcagggt agcttgcttt ggccggcgcg caaccctct gggggggccag
1381 ggcattggcc cc

```

(B) Homo Sapiens - JNKK2 (protein)
Accession AAB97813

```

1 maassleqkl srleaklkqe nrearrridl nldispqrpr ptlqlpland ggsrspsses
61 spqhptppar prhmlglpst lftprsmesi eidhklqeim kqtgyltigg qryqaeindl
121 enlgemsgst cgpvwkmrfr ktghviavkq mrrsgnkeen krilmlddv lkshdcpvkv
181 qcftgtfitnt dvfiamelmg tcaeklkkrm qgpiperilg kmtvaiivkal yylkkehgv
241 hrdvkpsnil ldergqiklc dfgisgrlvd skaktrsagc aaymaperid pdpptkpdvd
301 iradvwslgi slvelatgqf pykncktdfe vltkvlqcep pllpgmgfs gdfqsfvkd
361 ltkdhrkrpk ynkllhsfi kryetlevdv aswfkdvma t

```

FIG. 31 (A-B)

(C) Mus Musculus - JNKK2 (cDNA)
Accession: NM_011944

```

1  gggtgtcaga ctcaacgcag tgagtctgta aaaggctcta acatgcagga gcctttgacc
61  tcgtgccgaa ttcggcacga gggaggatcg acctcaactt ggatatcagc ccacagcggc
121 ccaggccccc cctgcaactc ccactggcca acgatggggg cagccgctca ccatacctcag
181 agagctcccc acagcaccct acacccccca cccggccccg ccacatgctg gggctcccat
241 caaccttggt cacaccgcgc agtatggaga gcatcgagat tgaccagaag ctgcaggaga
301 tcatgaagca gacagggtac ctgactatcg ggggccacgc ttatcaggga gaaatcaatg
361 acttgagaaa cttgggtgag atgggcagtg gtacctgtgg tcaggtgtgg aagatgcggt
421 tccggaagac aggccacatc attgctgtta agcaaatgcg gcgctctggg aacaaggaag
481 agaataagcg ctttttgatg gacctggatg tagtactcaa gagccatgac tgcccttaca
541 tcgttcagtg ctttggcacc ttcatcacca acacagacgt ctttattgcc atggagctca
601 tgggcatatg tgcagagaag ctgaagaaac gaatgcaggg cccatttcca gagcgaatcc
661 tgggcaagat gactgtggcg attgtgaaag cactgtacta tctgaaggag aagcatggcg
721 tcatccatcg cgatgtcaaa cctccaaca tctgtctaga tgagcggggc cagatcaagc
781 tctgtgactt tggcatcagt ggcgccttg ttgactccaa agccaaaaca cggagtgtcg
841 gctgtgctgc ctatatggct cccgagcgca tcgacctcc agatcccacc aagcctgact
901 atgacatccg agctgatgtg tggagcctgg gcactctact ggtggagctg gcaacaggac
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1321 ccccaacctg gccaacccag ctgcccacatc ggggacctgg ggacctggac gactgccaag
1381 gactgaggac agaaagtagg gggttcccat ccagctctga ctccctgcct accagctgtg
1441 gacaaaaggg catgctgggt cctaaccct cccactctgg ggtcagccag cagtgtgagc
1501 cccatcccac cccgacagac actgtgaacg gaagacagca ggccatgagc agactcgcta
1561 tttattcaat cataacctct gggctggggg aacccccagg ggcagagaga cggcacgagc
1621 tcaaaccaac tctgagtatg gaactctcag gctctctgaa ctctgacctt atctcctgga
1681 ctcactcacc aacagtgacc acttggtatc ttaacagacc tcagcacttc cagcacactg
1741 ctggtgggag ccttgcactc actatagtct caaacacaac aacaacaaca acaataataa
1801 caacaacaac aacaacaaca acaagctgcc tctgggttagc ttactgcatg cttccctcag
1861 ctcttgagta tcgctttctg ggagggttcc tcgaggtccc tggacggatg acttcccagc
1921 atcgttcact gcacttacta tgcactgaca taatatgcac cacattttgt gattgcaaga
1981 tacacatttg tcttaaaatt tgccacagct gaaacaaaag gtatatataa ggtataacgt
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2101 tatcaactgg aggaaactgt tcaagtgttc tgttttagacc aactgggaca gaaaacagat
2161 acctatgggg tgaggttcct attctcaggg tttgtttgtt tgtttgtttg tttgtttgtt
2221 tttcagtgc aattagagac agttcatggt ttcttgcaat tgtttttttc tggggggata
2281 attctggctt tgtttatctc tcgtgccgaa ttc

```

FIG. 31 (C)

(D) Mus Musculus - JNKK2 (protein)

Accession: NP_036074

```
1  mlglpstlft prsmesieid qklqeimkqt gyltiggqry qaeindlenl gemsgstcgq
61  vwkmrfrktg hiiavkqmrr sgnkeencri lmdldvvlks hdcpyivqcf gtfitntdvf
121 iamelmgica eklkkrmqgp iperilgkmt vaivkalyyl kekhgvihrd vkpsnillde
181 rgqiklcdfg isgrlvdska ktrsagcaay maperidppd ptkpdydira dvwslgislv
241 elatgqfpyk ncktdfevlt kvlqeeppll pghmgfsgdf qsfvkdcltk dhrkrpkynk
301 llehsfikhy eilevdvasw fkdvmaktds prtsgvlsqh hlpffr
```

FIG. 31 (D)